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In Vivo Distribution Dynamics of Gold Nanoparticles: A Quantitative Analysis

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1. Introduction

Advances in biomedical nanotechnology have spurred extensive research into gold nanoparticles (AuNPs) due to their unique properties that make them suitable for applications such as diagnostics, photothermal therapy, and targeted drug delivery. The surface functionalization of AuNPs allows for the modulation of their interactions with biological systems, which is crucial for optimizing biodistribution and minimizing toxic effects. This study aims to investigate the biodistribution of gum arabic (GA) functionalized AuNPs in Balb/C Nude mice following intravenous administration, in two dosage regimens (200 µCi and 600 µCi) and two time periods (3 and 24 hours). Observations highlight significant accumulation in the gallbladder, in addition to variations in biodistribution profiles that underscore the relevance of dose and time in the tissue distribution of AuNPs. Previous studies reinforce the importance of a detailed understanding of the pharmacokinetics and biodistribution of AuNPs to ensure their clinical applicability and safety, identifying primary accumulation in organs such as the liver and spleen, and assessing potential late toxic effects [1, 2, 3].

2. Methodology

Synthesis of AuNPs GA: Gold nanoparticles were synthesized using chloroauric acid (H198AuCl4) in a closed system with air filtration to prevent contamination. Gold irradiated in the EA-R1 nuclear reactor at IPEN was used to ensure isotopic purity. Reagents such as nitric acid, sodium hydroxide, sodium citrate, gum arabic, and ultrapure water were employed. Functionalization with gum arabic was carried out at 100 ºC, followed by the addition of NaOH and sodium citrate to form the NPs.

Animal Selection/Study Biodistribution: The research used rodents of the BALB/C Nude lineage, obtained from the IPEN vivarium (Institute for Energy and Nuclear Research), following guidelines approved by the CEUA (Ethics Committee on the Use of Animals) under number 243. /19. These mice were used to evaluate the biodistribution of GA AuNPs. Each animal was injected with 100 µL of AuNPs GA solution through the tail vein. The groups were organized according to dosage and post-injection time (200 µCi and 600 µCi evaluated at 3 and 24 hours). After administration, the animals were anesthetized with isoflurane and a 30 µL blood sample was collected by the retro-orbital method. The organs were stored in labeled tubes for quantitative analysis with a gamma counter, determining the biodistribution of the nanoparticles in %ID/g.

3. Results and Discussion

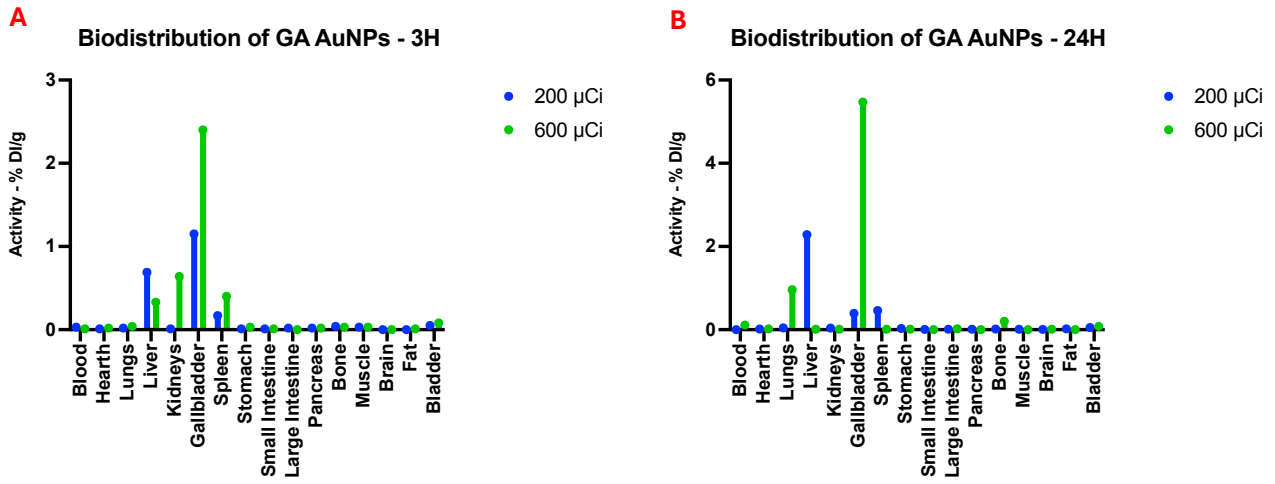

Figure 1: Biodistribution of Gum Arabic-Functionalized Gold Nanoparticles (AuNPs GA) in Balb/C Nude Mice. **Panel A** illustrates the biodistribution 3 hours post-intravenous injection, while **Panel B** depicts the biodistribution 24 hours after injection. Blue bars represent animals administered with 200 µCi and green bars represent those with 600 µCi. Notable uptake of nanoparticles in the gallbladder and liver is evident, with the comparative analysis across the two time points highlighting the dynamics of nanoparticle distribution and clearance.

The preferential accumulation in the gallbladder might represent an excretion route for AuNPs GA or a sequestration mechanism by the organ. The significant liver uptake corroborates literature identifying the liver as a primary site for nanoparticle accumulation following intravenous administration, likely due to opsonization and subsequent phagocytosis by the reticuloendothelial system. The variation in biodistribution between doses indicates that the injected quantity of AuNPs GA directly influences the distribution profile within the body.

Biodistribution results after 24 hours suggest clearance of AuNPs GA from the liver, with a decrease in detected activity percentage. This could be due to biotransformation or biliary excretion of the nanoparticles. The increased activity percentage in the gallbladder for the 600 µCi samples after 24 hours further supports the biliary excretion hypothesis.

These findings are crucial for understanding the fate of gold nanoparticles post-intravenous administration and can aid in designing AuNPs with optimized biodistribution properties for specific clinical applications. Additionally, the low uptake in the brain and adipose tissue is favorable from a safety perspective, minimizing the risk of adverse effects in non-target organs.

This study aligns with existing literature and enhances our understanding of AuNPs interactions with biological systems, a critical aspect for advancing nanomedicine. Continued exploration of the underlying mechanisms of nanoparticle biodistribution and excretion can lead to significant advancements in targeted therapy and medical imaging.

Interestingly, intratumoral administration of AuNPs GA, as presented by Barbezan et al., 2024, showed a more favorable biodistribution profile, with less accumulation in vital organs. This delivery method resulted in significantly higher concentration in tumor cells, with reduced uptake by non-target organs, as illustrated in recent results [4].

Direct intratumoral administration ensures that a larger fraction of the administered dose remains at the tumor site, potentially increasing therapeutic efficacy and reducing systemic toxicity. Compared to intravenous administration, as performed in this study, there might be rapid absorption by the reticuloendothelial system, particularly in the liver, as observed in the 3 and 24-hour samples.

The data underscore the importance of considering the administration route in designing therapeutic strategies using AuNPs. Strategies that minimize exposure to non-target organs and maximize tumor delivery are essential for advancing the clinical use of nanoparticles in medicine. The comparison with Barbezan et al.'s data highlights the need to optimize the delivery route for more efficient and safer treatments.

4. Conclusions

The study of the biodistribution of radioactive gum arabic-functionalized gold nanoparticles (AuNPs GA) revealed significant accumulation in the liver and gallbladder, supporting the hypothesis of biliary excretion, particularly at higher dosages. Notably, unlike the study by Barbezan et al., 2024, which investigated AuNPs BSA in tumor-bearing animals, the current study focused on tumor-free mice to solely assess the distribution dynamics of AuNPs GA. This specific design was chosen to purely understand the distribution behavior of nanoparticles without the variables introduced by tumor pathologies. These insights enhance our knowledge of nanoparticle behavior in the body and are essential for refining delivery strategies and functionalization of AuNPs for clinical use.

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